

Serial No.: 10/057,467

Filed: January 22, 2002

**In the Claims:**

Please cancel claims 1-7, without prejudice or disclaimer.

Please add the following new claims:

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-8. (New) A method for in vitro screening for a transdominant intracellular bioactive agent capable of altering the phenotype of a cell, said method comprising the steps:

- A1
- a) introducing a molecular library of retroviral vectors comprising randomized candidate nucleic acids into a plurality of cells, wherein each of said nucleic acids comprises a different nucleotide sequence, wherein said randomized candidate nucleic acids are expressed in said cells to produce a plurality of randomized peptides, wherein each of said retroviral vectors comprises a nucleic acid encoding at least one glycine N-terminal to the randomized peptide;
  - b) screening said plurality of cells for a cell exhibiting an altered phenotype, wherein said altered phenotype is due to the presence of a transdominant bioactive agent; and
  - c) identifying said transdominant bioactive agent.

9. (New) A method according to claim 8 wherein said identifying comprises:

- i) isolating said cell exhibiting an altered phenotype.

10. (New) A method according to claim 9 wherein said identifying further comprises:

- ii) sequencing said nucleic acid encoding said transdominant bioactive agent.

11. (New) A method according to claim 8 wherein each of said nucleic acids further comprise a presentation sequence capable of presenting said expression product in a conformationally restricted form.

12. (New) A method according to claim 8 wherein said cells are mammalian cells.

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13. (New) A method according to claim 8 wherein said library comprises at least  $10^4$  different nucleic acids.

14. (New) A method according to claim 8 wherein said library comprises at least  $10^5$  different nucleic acids.

15. (New) A method according to claim 8 wherein said library comprises at least  $10^6$  different nucleic acids.

16. (New) A method according to claim 8 wherein said library comprises at least  $10^7$  different nucleic acids.

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17. (New) A method according to claim 8 wherein said library comprises at least  $10^8$  different nucleic acids.

18. (New) A method according to claim 8 wherein said library comprises at least  $10^9$  different nucleic acids.

19. (New) A method according to claim 8 wherein each of said candidate nucleic acids is linked to nucleic acid encoding at least one fusion partner.

20. (New) A method according to claim 19 wherein said fusion partner comprises a nuclear localization signal sequence.

21. (New) A method for in vitro screening for a transdominant intracellular bioactive agent capable of altering the phenotype of a cell, said method comprising the steps:

- a) introducing a molecular library of retroviral vectors comprising randomized candidate nucleic acids into a plurality of cells, wherein each of said nucleic acids

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comprises a different nucleotide sequence, wherein said randomized candidate nucleic acids are expressed in said cells to produce a plurality of randomized peptides;

- b) screening said plurality of cells for a cell exhibiting an altered phenotype, wherein said altered phenotype is due to the presence of a transdominant bioactive agent, wherein said altered phenotype is cell growth; and
- c) identifying said transdominant bioactive agent.

22. (New) A method for in vitro screening for a transdominant intracellular bioactive agent capable of altering the phenotype of a cell, said method comprising the steps:

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- a) introducing a molecular library of retroviral vectors comprising randomized candidate nucleic acids into a plurality of cells, wherein each of said nucleic acids comprises a different nucleotide sequence, wherein said randomized candidate nucleic acids are expressed in said cells to produce a plurality of randomized peptides;
  - b) screening said plurality of cells for a cell exhibiting an altered phenotype, wherein said altered phenotype is due to the presence of a transdominant bioactive agent, wherein said altered phenotype is cell death; and
  - c) identifying said transdominant bioactive agent.

23. (New) A method for in vitro screening for a transdominant intracellular bioactive agent capable of altering the phenotype of a cell, said method comprising the steps:

- a) introducing a molecular library of retroviral vectors comprising randomized candidate nucleic acids into a plurality of cells, wherein each of said nucleic acids comprises a different nucleotide sequence, wherein said randomized candidate nucleic acids are expressed in said cells to produce a plurality of randomized peptides;

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- b) screening said plurality of cells for a cell exhibiting an altered phenotype, wherein said altered phenotype is due to the presence of a transdominant bioactive agent, wherein said altered phenotype is a change in expression of cellular differentiation markers; and
  - c) identifying said transdominant bioactive agent.

24. (New) The method according to claim 23, wherein said cellular differentiation markers are characteristic of T-cell activation.

25. (New) The method according to claim 23, wherein said cellular differentiation markers are characteristic of B-cell activation.--

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